A Novel Hybrid Compound LLP2A-Ale Both Prevented and Rescued the Osteoporotic Phenotype in a Mouse Model of Glucocorticoid-Induced Osteoporosis.

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Public Summary:
LLP2A-Ale is a novel bone-seeking compound that recruits mesenchymal stem cells to the bone surface, stimulates bone formation, and increases bone mass. Prolonged glucocorticoid (GC) administration causes secondary osteoporosis (GIOP) and non-traumatic osteonecrosis. The purpose of this study was to determine if treatment with LLP2A-Ale alone or in combination with parathyroid hormone (PTH) could prevent or treat GIOP in a mouse model.

Scientific Abstract:
Prolonged glucocorticoid (GC) administration causes secondary osteoporosis (GIOP) and non-traumatic osteonecrosis. LLP2A-Ale is a novel bone-seeking compound that recruits mesenchymal stem cells to the bone surface, stimulates bone formation, and increases bone mass. The purpose of this study was to determine if treatment with LLP2A-Ale alone or in combination with parathyroid hormone (PTH) could prevent or treat GIOP in a mouse model. Four-month-old male Swiss-Webster mice were randomized to a prevention study with placebo, GC (day 1-28), and GC + LLP2A-Ale (IV, day 1) or a treatment study with placebo, GC (days 1-56), GC + LLP2A-Ale (IV, day 28), GC + PTH, and GC + LLP2A-Ale + PTH (days 28-56). Mice were killed on day 28 (prevention study) or on day 56 (treatment study). The study endpoints included bone mass, bone strength, serum markers of bone turnover (P1NP and CTX-I) and angiogenesis (VEGF-A), surface-based bone turnover, and blood vessel density. LLP2A-Ale prevented GC-induced bone loss and increased mechanical strength in the vertebral body (days 28 and 56) and femur (day 56). LLP2A-Ale, PTH, and LLP2A-Ale + PTH treatment significantly increased the mineralizing surface, bone formation rate, mineral apposition rate, double-labeled surface, and serum P1NP level on day 56. LLP2A-Ale and PTH treatment increased femoral blood vessel density and LLP2A-Ale increased serum VEGF-A on day 28. Therefore, LLP2A-Ale monotherapy could be a potential option to both prevent and treat GC-induced osteoporosis and bone fragility.